VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning at line 2 of page 1 has been amended as follows:

The present application is a [Continuation-In-Part application of U.S. Patent Appln. Ser. No. 08/________, filed 04/18/97, which is a Continuation-in-Part of U.S. Patent Appln. Ser. No. 08/724,643, filed on October 1, 1996] continuation of U.S. Patent Application No. 08/846,017, filed April 25, 1997, abandoned; which is a continuation-in-part of U.S. Patent Application No. 08/844, 419, filed April 18, 1997, abandoned; which is a continuation-in-part of U.S. Patent Application No. .08/724,643 filed October 1, 1996, abandoned; each of which is incorporated herein by reference in its entirety.

The paragraph beginning at line 6 of page 10 has been amended as follows:

The present invention further provides substantially purified polypeptides comprising the amino acid sequence comprising SEQ ID NOS:[61,] 63, 64, 65, 67, and [68] 69. In another embodiment, the present invention also provides purified, isolated polynucleotide sequences encoding the polypeptides comprising the amino acid sequences of SEQ ID NOS:[61,] 63, 64, 65, 67, and [68] 69. The present invention contemplates portions or fragments of SEQ ID NOS:[61,] 63, 64, 65, 67, and [68] 69, of various lengths. In one embodiment, the portion of polypeptide comprises fragments of lengths greater than 10 amino acids. However, the present invention also contemplates polypeptide sequences of various lengths, the sequences of which are included within SEQ ID NOS:61, 63, 64, 65, 67, and [68] 69, ranging from 5 to 500 amino acids (as appropriate, based on the length of SEQ ID NOS:[61,] 63, 64, 65, 67, and [68] 69).

The paragraph beginning at line 17 of page 10 has been amended as follows:

The present invention also provides nucleic acid sequences comprising SEQ ID NOS:55, 62, 66, and [69] 68, or variants thereof. The present invention further provides fragments of the isolated polynucleotide sequences that are at least 6 nucleotides, at least 25 nucleotides, at least 30 nucleotides, at least 50 nucleotides, at least 100 nucleotides, at least 250 nucleotides, and at least 500 nucleotides in length (as appropriate for the length of the sequence of SEQ ID NOS:55, 62, 66, and [69] 68, or variants thereof).

The paragraph beginning at line 24 of page 10 has been amended as follows:

In particularly preferred embodiments, the polynucleotide hybridizes specifically to telomerase sequences, wherein the telomerase sequences are selected from the group consisting of human, *Euplotes aediculatus*, *Oxytricha, Schizosaccharomyces*, and *Saccharomyces* telomerase sequences. In other preferred embodiments, the present invention provides polynucleotide sequences comprising the complement of nucleic acid sequences selected from the group consisting of SEQ ID NOS:55, 62, 66, and [69] 68, or variants thereof. In yet other preferred embodiments, the present invention provides polynucleic acid sequences that hybridize under stringent conditions to at least one nucleic acid sequence selected from the group consisting of SEQ ID NOS:55, 62, 66, and [69] 68. In a further embodiment, the polynucleotide sequence comprises a purified, synthetic nucleotide sequence having a length of about ten to thirty nucleotides.

The paragraph beginning at line 21 of page 11 has been amended as follows:

The present invention also provides antisense molecules comprising the nucleic acid sequence complementary to at least a portion of the polynucleotide of SEQ ID NOS:55, 62, 66, 67, and [69] 68. In an alternatively preferred embodiment, the present invention also provides pharmaceutical compositions comprising antisense molecules of SEQ ID NOS:55, 62, 67, and [69] 68, and a pharmaceutically acceptable excipient and/or other compound (*e.g.,* adjuvant).

The paragraph beginning at line 1 of page 12 has been amended as follows:

The present invention also provides methods for producing polypeptides comprising the amino acid sequence of SEQ ID NOS:61, 63, 65, 67, or [69] 68, the method comprising the steps of: culturing a host cell under conditions suitable for the expression of the polypeptide; and recovering the polypeptide from the host cell culture.

The paragraph beginning at line 6 of page 12 has been amended as follows:

The present invention also provides purified antibodies that binds specifically to a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NOS:55, [61,] 63, 64, 65, 67, and/or [68] 69. In one embodiment, the present invention provides a pharmaceutical composition comprising at least one antibody, and a pharmaceutically acceptable excipient.

The paragraph beginning at line 11 of page 12 has been amended as follows:

The present invention further provides methods for the detection of human telomerase in a biological sample comprising the steps of: providing a biological sample suspected of expressing human telomerase protein; and at least one antibody that binds specifically to at least a portion of the amino acid sequence of SEQ ID NOS:55, [61,] 63, 64, 65, 67, and/or [68] 69; combining the biological sample and antibody(ies) under conditions such that an antibody:protein complex is formed; and detecting the complex wherein the presence of the complex correlates with the expression of the protein in the biological sample.

The paragraph beginning at line 19 of page 12 has been amended as follows:

The present invention further provides substantially purified peptides comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:71, 73, 75, 77, 79, 82, 83,[83,] 85, [86], and 101. In an alternative embodiment, the present invention provides purified, isolated polynucleotide sequences encoding the polypeptide corresponding to these sequences. In preferred embodiments, the polynucleotide hybridizes specifically to telomerase sequences, wherein the telomerase sequences are selected from the group consisting of human, *Euplotes aediculatus*, *Oxytricha, Schizosaccharomyces*, and *Saccharomyces* telomerase sequences. In yet another embodiment, the polynucleotide sequence comprises the complement of a nucleic acid sequence selected from the group consisting of SEQ ID NOS:70, 72, 74, 76, 78, 80, 81, and 100, and variants thereof. In a further embodiment, the polynucleotide sequence that hybridizes under stringent conditions to a nucleic acid sequence selected from the group consisting of SEQ ID NOS:66, [69] 68, 80, and 81. In yet another embodiment, the polynucleotide sequence is selected from the group consisting of SEQ ID NOS:70, 72, 74, 76, 78, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 102, 103, 104, 105, 106, 107, 108, 109, and 110. In an alternative embodiment, the nucleotide sequence comprises a purified, synthetic nucleotide sequence having a length of about ten to fifty nucleotides.

The paragraph beginning at line 22 of page 13 has been amended as follows::

The present invention also provides antisense molecules comprising the nucleic acid sequence complementary to at least a portion of the polynucleotide of SEQ IDS NOS:82 and 100. In an alternatively preferred embodiment, the present invention also provides pharmaceutical

PATENT

compositions comprising antisense molecules of SEQ ID NOS:82 and 100, and a pharmaceutically acceptable excipient and/or other compound (*e.g.,* adjuvant).

The paragraph beginning at line 3 of page 14 has been amended as follows:

The present invention also provides methods for producing polypeptides comprising the amino acid sequence of SEQ ID NOS:82, 83, 84, 85, [86,] and 101, the method comprising the steps of: culturing a host cell under conditions suitable for the expression of the polypeptide; and recovering the polypeptide from the host cell culture.

The paragraph beginning at line 8 of page 14 has been amended as follows:

The present invention also provides purified antibodies that binds specifically to a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NOS:71, 73, 75, 77, 79, 82, 83, 84, 85, [86,] and/or 101. In one embodiment, the present invention provides a pharmaceutical composition comprising at least one antibody, and a pharmaceutically acceptable excipient.

The paragraph beginning at line 13 of page 14 has been amended as follows:

The present invention further provides methods for the detection of human telomerase in a biological sample comprising the steps of: providing a biological sample suspected of expressing human telomerase protein; and at least one antibody that binds specifically to at least a portion of the amino acid sequence of SEQ ID NOS:71, 73, 75, 77, 79, 82, 83, 84, 85, [86,] 87, and/or 101; combining the biological sample and antibody(ies) under conditions such that an antibody:protein complex is formed; and detecting the complex wherein the presence of the complex correlates with the expression of the protein in the biological sample.

The paragraph beginning at line 18 of page 16 has been amended as follows:

Figure 25 shows the alignment of the human telomere amino acid motifs (SEQ ID NO:[61] 67), with portions of the tez1 sequence (SEQ ID NO:63), Est2p (SEQ ID NO:64), and the *Euplotes* p123 (SEQ ID NO:65).

The paragraph beginning at line 26 of page 16 has been amended as follows:

PATENT

Figure 29 shows the amino acid sequence of *tez1* (SEQ ID NO:[68] 69).

The paragraph beginning at line 27 of page 16 has been amended as follows:

Figure 30 shows the DNA sequence of *tez1* (SEQ ID NO:[69] 68).

The paragraph beginning at line 1 of page 17 has been amended as follows:

Figure 32 (SEQ ID NOS:112-117) shows the sequences of peptides useful for production of antibodies.

The paragraph beginning at line 3 of page 17 has been amended as follows:

Figure 34 (SEQ ID NOS:118-121) shows two degenerate primers used in PCR to identify the *S. pombe* homolog of the *E. aediculatus* p123 sequences.

The paragraph beginning at line 5 of page 17 has been amended as follows:

Figure 35 (SEQ ID NOS:119, 121) shows the four major bands produced in PCR using the degenerate primers.

The paragraph beginning at line 7 of page 17 has been amended as follows:

Figure 36 (SEQ ID NOS: 58, 118, 121-130) shows the alignment of the M2 PCR product with *E. aediculatus* p123, *S. cerevisiae*, and *Oxytricha* telomerase protein sequences.

The paragraph beginning at line 9 of page 17 has been amended as follows:

Figure 37 (SEQ ID NOS:131-132) is a schematic showing the 3' RT PCR strategy.

The paragraph beginning at line 15 of page 17 has been amended as follows:

Figure 41 (SEQ ID NOS: 133-147) shows the alignment of RT domains from telomerase catalytic subunits.

The paragraph beginning at line 17 of page 17 has been amended as follows:

Figure 42 (SEQ ID NOS: 2, 55, 69) shows the alignment of three telomerase sequences.

The paragraph beginning at line 25 of page 17 has been amended as follows:

Figure 47 (SEQ ID NOS: 100-101) shows the DNA (SEQ ID NO:100) and amino acid (SEQ ID NO:101) of the ORF encoding an approximately 63 kDa telomerase protein or fragment thereof.

The paragraph beginning at line 28 of page 17 has been amended as follows:

Figure 48 (SEQ ID NOS: 148-171) shows an alignment of reverse transcriptase motifs from various sources.